Uniaxial mechanical strain modulates the differentiation of neural crest stem cells into smooth muscle lineage on micropatterned surfaces.

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Public Summary:
Neural crest stem cells (NCSCs) play an important role in development and represent a valuable cell source for tissue engineering. In this study, NCSCs were derived from induced pluripotent stem cells and used as a model to determine whether vascular mechanical strain modulates the differentiation of NCSCs into the smooth muscle (SM) lineage. NCSCs were cultured on micropatterned membranes to mimic the organization of smooth muscle cells (SMCs), and subjected to cyclic uniaxial strain. Mechanical strain enhanced NCSC proliferation and the appearance of SM markers. Conversely, mechanical strain suppressed the differentiation of NCSCs into Schwann cells. Our results demonstrated that mechanical strain regulates the differentiation of NCSCs in a manner dependent on biochemical factors and the differentiation stage of NCSCs. Understanding the mechanical regulation of NCSC differentiation will shed light on the development and remodeling of vascular tissues, and how transplanted NCSCs respond to mechanical factors.

Scientific Abstract:
Neural crest stem cells (NCSCs) play an important role in the development and represent a valuable cell source for tissue engineering. However, how mechanical factors in vivo regulate NCSC differentiation is not understood. Here NCSCs were derived from induced pluripotent stem cells and used as a model to determine whether vascular mechanical strain modulates the differentiation of NCSCs into smooth muscle (SM) lineage. NCSCs were cultured on micropatterned membranes to mimic the organization of smooth muscle cells (SMCs), and subjected to cyclic uniaxial strain. Mechanical strain enhanced NCSC proliferation and ERK2 phosphorylation. In addition, mechanical strain induced contractile marker calponin-1 within 2 days and slightly induced SM myosin within 5 days. On the other hand, mechanical strain suppressed the differentiation of NCSCs into Schwann cells. The induction of calponin-1 by mechanical strain was inhibited by neural induction medium but further enhanced by TGF-beta. For NCSCs pre-treated with TGF-beta, mechanical strain induced the gene expression of both calponin-1 and SM myosin. Our results demonstrated that mechanical strain regulates the differentiation of NCSCs in a manner dependent on biochemical factors and the differentiation stage of NCSCs. Understanding the mechanical regulation of NCSC differentiation will shed light on the development and remodeling of vascular tissues, and how transplanted NCSCs respond to mechanical factors.